REMARKS

AMENDMENTS

Claims 19-28 and 33 are canceled herein, claims 29-35 are amended, and new claim 36 is added. Support for the amendments to claims 29-31 is found at p.4:23-27, for claim 32 at p.5:43-46, and for claims 34-36 at p.14:6-28.

Applicants have amended the paragraph beginning on page 3, line 41 of the specification. The title of the application has been amended to indicate the subject matter of the claims to be a process for treating migraine disorders using 5-HT5 binding partners.

RESTRICTION REQUIREMENT

Applicants respectfully reassert their view of claims 19-36 being related through the binding partners of 5-HT5 receptors, which define the claims, as a whole, over the prior art. Nevertheless, with a view to facilitating prosecution, applicants have canceled claims 19-28.

INDEFINITENESS REJECTION UNDER 35 USC §112, ¶2

Applicants respectfully submit that the amendments to claims 29, 30, and 35 are sufficient to overcome the examiner's rejections thereof.

ENABLEMENT REJECTION UNDER 35 USC §112, ¶1

The examiner rejects claims 29-35 under 35 USC §112, ¶1 for lack of

enablement. This rejection is respectfully traversed.

The examiner's arguments focus on prior art recognition of the role played by 5-HT1D receptors in the treatment of migraine disorders. As the examiner has correctly set forward, much evidence exists to implicate these receptors in what has been termed the "vascular theory" of migraine causation (*see* specification at p.2:12-14). In addition, however, the prior art also recognizes at least one other theory for migrane causation, the "neurogenic theory" (*see* specification at p.2:14-19). Further, the precise mechanism of action underlying migrane disorders has not been definitively established. Accordingly, the examiner's analysis based on 5-HT1D receptor distribution may not be thoroughly conclusive.

The present specification sets forward several "animal models [based] on mechanisms which can underlie the formation of migraine" disorders (p.11:28-30). These animal models include protein extravasation, distribution of carotid blood flow, measurement of the nitroglycerin-induced c-fos gene expression and translocation, measurement of other transcription factors such as c-jun, zif268, or Homer gene isoforms, retinal spreading depression, and cortical spreading depression (*see* specification at p.7:15-21 and p.11:32-12:20). These animal models are described in detail in the prior art, and testing identified 5-HT5 binding partners using these models would be a matter of routine to the appropriately skilled artisan.

The specification contains assertions as to the efficacy of 5-HT5 binding partners in treating migraine disorders which must be taken as enabling in the absence of specific reasoning to the contrary. The reasoning so far presented by the examiner

does not account for all information available to one of skill in the art, and may not be, therefore, sufficient to overcome the established presumption.

To further prosecution, however, applicants include herewith a copy of a declaration, duly executed by the inventor, the original of which will be supplied directly, which demonstrates the efficacy of 5-HT5 binding partners in an appropriate animal model. The completed experiments measure retinal spreading depression, and are based on mechanisms underlying migraine disorder causation. The obtained results demonstrate clearly that selective 5-HT5 binding partners are effective in this animal model, and further demonstrate that 5-HT5 binding partners are *more* effective with regard to this model than the 5-HT1D binding partner sumatriptan.

Applicants respectfully submit that the declaration demonstrates that one of skill in the art would be able to carry out the presently claimed invention based on the specification disclosure and knowledge held in the art. It is respectfully requested that the rejection of claims 29-35 under 35 USC §112, ¶1 for lack of enablement, be withdrawn.

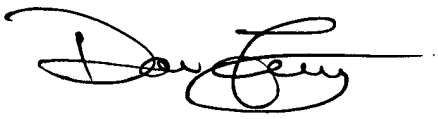
CONCLUSION

In view of the foregoing amendments and remarks, applicants consider that the rejections of record have been obviated and respectfully solicit passage of the application to issue.

Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees to Deposit Account No. 11-0345. Please credit

any excess fees to such deposit account.

Respectfully submitted,
KEIL & WEINKAUF



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AMENDMENTS TO THE SPECIFICATION

Please amend the title to read as follows:

Use of 5-HT5 receptor binding ~~Binding~~ partners ~~for 5-HT5 receptors~~ for migraine treatment

Please amend the paragraph found on page 3, at lines 41-45, to read as follows:

~~or include metal complex-like coordinative bonds. [sic]~~ In addition to the abovementioned, reversible molecular interactions, irreversible interactions between binding partner and receptor can also be possible, such as, for example, covalent bonds.

COPY OF ALL CLAIMS

1-28 (canceled)

29. (currently amended) A method for treating migrainous cerebrovascular disorders which comprises administering to a subject in need thereof an effective amount of at least one binding partner for a 5-HT5-receptor ~~5-HT5-receptors~~ whose binding affinity for the 5-HT5-receptor ~~5-HT5-receptors~~ is at least 10 times greater than its binding affinity for a 5-HT1D-receptor ~~5-HT1D-receptors~~.

30. (currently amended) The method as claimed in claim 29, where the binding affinity of the binding partner for a 5-HT5-receptor ~~5-HT5-receptors~~ is at least 20 times greater ~~by at least the factor 2~~ than its binding affinity for a 5-HT1D-receptor ~~5-HT1D-receptors~~.

31. (currently amended) The method as claimed in claim 29, where the binding affinity of the binding partner for a 5-HT5-receptor ~~5-HT5-receptors~~ is at least 50 times greater ~~by at least the factor 5~~ than its binding affinity for a 5-HT1D-receptor ~~5-HT1D-receptors~~.

32. (currently amended) The method as claimed in claim 29, where the K_i value for binding of the binding partner to the 5-HT5-receptor ~~5-HT5-receptors~~ is ~~also~~ less than 10^{-8} M.

33. (canceled)

34. (currently amended) The method as claimed in claim 29, wherein the migrainous cerebrovascular disorder is ~~for the treatment of~~ migraine.

35. (currently amended) The method as claimed in claim 34, wherein the binding partner is administered when acute symptoms of migraine occur ~~for the acute treatment of migraine~~.

36. (new) The method as claimed in claim 34, wherein the migraine is a disorder selected from the group consisting of associated migraine, migraine equivalents, digestive migraine, ophthalmic migraine, ophthalmoplegic migraine, migraine rouge, cluster headache and cervical migraine.